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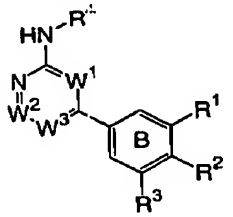
Applicants: Randy S. Bethiel et al.
Application No.: 10/700,936

AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Previously presented) A compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

W^1 is nitrogen or CH, W^2 is nitrogen or C-$(U)_pR^U$, and W^3 is nitrogen or C-$(V)_qR^V$;

p and q are each independently 0 or 1;

R^U and R^V are each independently R or Ar^1;

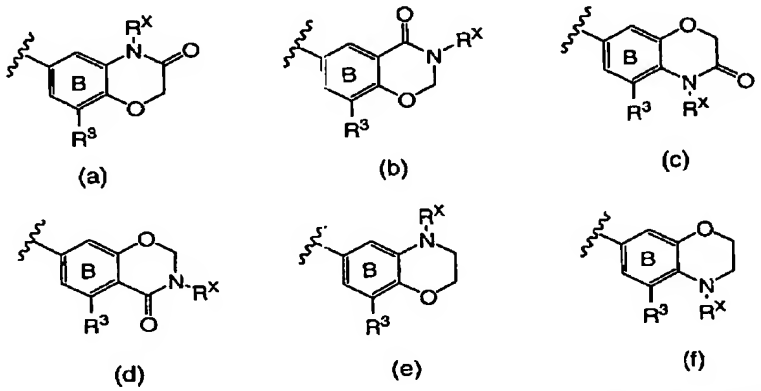
U and V are each independently a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

each occurrence of R is independently hydrogen or an optionally substituted C_1-C_4 aliphatic, or two R bound to the same nitrogen atom are optionally taken together with the nitrogen atom to form a 3-7 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Ar^1 is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or

sulfur; wherein Ar^1 is optionally substituted with m independent occurrences of Z-R^5; wherein m is 0-5, Z is a bond or is a C_1-C_6 alkylidene chain wherein up to two methylene units of Z are optionally replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR; and each occurrence of R^5 is independently hydrogen, an optionally substituted aliphatic, heteroaliphatic, aryl or heteroaryl group, halogen, NO_2, CN, OR, SR, $N(R)_2$, NRCOR, $NRCON(R)_2$, $NRCO_2R$, COR, CO_2R, OCOR, $CON(R)_2$, $OCON(R)_2$, SOR, SO_2R, $SO_2N(R)_2$, $NRSO_2R$, $NRSO_2N(R)_2$, COCOR, or $COCH_2COR$;

R^1 and R^2 are taken together and fused to ring B to form a heterocyclic moiety selected from one of formulae (a) through (f):



wherein each occurrence of R^X is independently hydrogen, QR, or Q_nAr^1; n is zero or one; and Q is an optionally substituted C_{1-4} alkylidene chain wherein one methylene unit of Q is optionally replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR;

R^3 is hydrogen, halogen, QR, Q_nCN, Q_nNO_2, or Q_nAr^1; and

R^4 is Ar^1, or T-Ar^1;

wherein T is a C_{1-2} alkylidene chain wherein one methylene unit of T is optionally replaced by CO, CO_2, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, $NRCO_2$, NRCONR, SO, SO_2, $NRSO_2$, SO_2NR, $NRSO_2NR$, O, S, or NR.

2. (Previously presented) The compound of claim 1, wherein R^1 and R^2 taken together form the heterocyclic moiety of formula (a) and R^X is hydrogen or optionally substituted C_{1-6} aliphatic.

3. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6}alkyl substituted with $N(R)_2$, or C_{1-6}alkyl substituted with Ar^1.

4. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, or C_{1-2}alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

5. (Original) The compound of claim 1, wherein R^3 is hydrogen, halogen, QR or QAr^1, wherein Q is a C_{1-3} alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar^1 is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

6. (Original) The compound of claim 1, wherein R^3 is hydrogen, OH, OCH_3, OCH_2CH_3, NHCOMe, NH_2, $NH(C_{1-4}$ aliphatic), $N(C_{1-4}$ aliphatic$)_2$, $O(CH_2)_2$morpholin-4-yl, $O(CH_2)_2NH_2$, $O(CH_2)_2NH(C_{1-4}$ aliphatic), $O(CH_2)_2N(C_{1-4}$ aliphatic$)_2$, Br, Cl, or F.

7. (Original) The compound of claim 1, wherein R^3 is hydrogen.

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8. (Original) The compound of claim 1, wherein R^4 is a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogen atoms, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted.

9. (Original) The compound of claim 1, wherein R^4 is optionally substituted phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl.

10. (Original) The compound of claim 1, wherein R^4 is an optionally substituted phenyl group.

11. (Original) The compound of claim 8, wherein each occurrence of Z is independently a bond or a C_{1-4} alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO_2-, or -NH-; and each occurrence of R^5 is independently hydrogen, C_{1-6} aliphatic, halogen, NO_2, OR, $N(R)_2$, or optionally substituted phenyl, pyridyl, or pyrimidinyl.

12. (Previously presented) The compound of claim 8, wherein each occurrence of ZR^5 is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF_3, NH_2, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO_2NH_2, $CONH_2$, CO_2Me, phenoxy, O-pyridinyl, SO_2phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF_3-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, and fluorophenoxy.

13. (Original) The compound of claim 1, wherein $(U)_pR^U$ and $(V)_qR^V$ are each independently hydrogen, halogen, NO_2, CN, OR, SR or $N(R)_2$, or C_{1-4}aliphatic optionally substituted with oxo, OR, SR, $N(R)_2$, halogen, NO_2 or CN.

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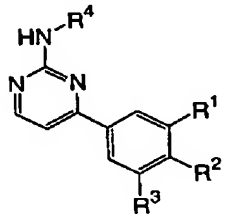
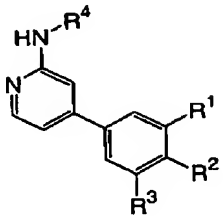
14. (Original) The compound of claim 1, wherein $(U)_pR^U$ and $(V)_qR^V$ are each independently hydrogen, Me, OH, or OMe.

15. (Original) The compound of claim 1, wherein W^1 is N or CH and compounds have the structure of Formula **Ia** or **Ib**:



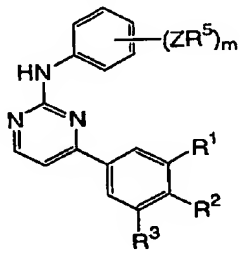
Ia



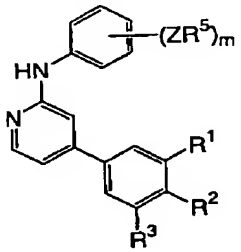
Ib

or a pharmaceutically acceptable salt thereof.

16. (Previously presented) The compound of claim 15, wherein R^4 is an optionally substituted phenyl group and compounds have the structure of Formula **IIa** or **IIb**:



IIa



IIb

or a pharmaceutically acceptable salt thereof.

17. (Previously presented) The compound of claim 16, wherein R^3 is hydrogen, and compounds have the structure of Formula **IIIa** or **IIIb**:

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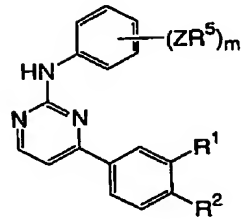
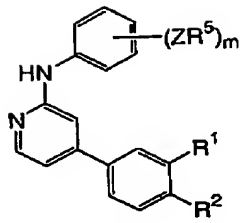


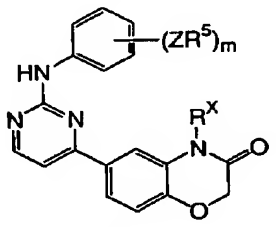
IIIa



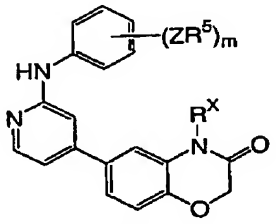
IIIb

or a pharmaceutically acceptable salt thereof.

18. (Previously presented) The compound of claim 16, wherein R^3 is hydrogen, and R^1 and R^2 taken together form the heterocyclic moiety of formula (a) and compounds have the structure of Formula **IVa** or **IVb:**



IVa



IVb

or a pharmaceutically acceptable salt thereof.

19. (Previously presented) The compound of claim 15, wherein

i) R^1 and R^2 taken together form the heterocyclic moiety of formula (a); where R^X is defined according to one of the following groups:

(a) hydrogen or optionally substituted C_{1-6}aliphatic;

(b) hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6}alkyl substituted with $N(R)_2$, or C_{1-6}alkyl substituted with Ar^1; or

(c) hydrogen, methyl, or C_{1-2}alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

ii) R^3 is defined according to one of the following groups:

(a) hydrogen, halogen, QR or QAr^1, wherein Q is a C_{1-3} alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar^1 is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

(b) hydrogen, OH, OCH_3, OCH_2CH_3, NHCOMe, NH_2, $NH(C_{1-4}$ aliphatic), $N(C_{1-4}$ aliphatic$)_2$, $O(CH_2)_2$morpholin-4-yl, $O(CH_2)_2NH_2$, $O(CH_2)_2NH(C_{1-4}$ aliphatic), $O(CH_2)_2N(C_{1-4}$ aliphatic$)_2$, bromo, chloro, or fluoro; or

(c) hydrogen;

iii) R^4 is defined according to one of the following groups:

(a) a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogens, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is optionally substituted with $(ZR^5)_m$;

(b) an optionally substituted ring selected from phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl, wherein said ring is optionally substituted with $(ZR^5)_m$; or

(c) an optionally substituted phenyl group, wherein said phenyl group is optionally substituted with $(ZR^5)_m$;

iv) W^1, W^2 and W^3 are defined according to one of the following groups:

(a) W^1 is nitrogen or CH, W^2 is nitrogen or $C\text{-}(U)_pR^U$, and W^3 is nitrogen or $C\text{-}(V)_qR^V$;

(b) W^1 is nitrogen or CH, W^2 is C-$(U)_pR^U$, and W^3 is C-$(V)_qR^V$; or

(c) W^1 is nitrogen or CH and W^2 and W^3 are each CH; and

v) $(U)_pR^U$ and $(V)_qR^V$ groups are defined according to one of the following groups:

(a) hydrogen, halogen, NO_2, CN, OR, SR or $N(R)_2$, or C_{1-4}aliphatic optionally substituted with oxo, OR, SR, $N(R)_2$, halogen, NO_2 or CN;

(b) hydrogen, Me, OH, OMe or $N(R)_2$; or

(c) both $(U)_pR^U$ and $(V)_qR^V$ are hydrogen.

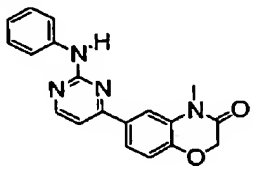
20. (Previously presented) The compound of any one of claims 16, 17, 18 or 19, wherein each occurrence of Z is independently a bond or a C_{1-4} alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, $-SO_2-$, or -NH-; and each occurrence of R^5 is independently hydrogen, C_{1-6} aliphatic, halogen, NO_2, OR, $N(R)_2$, or optionally substituted phenyl, pyridyl, and pyrimidinyl

21. (Previously presented) The compound of claim 20, wherein each occurrence of ZR^5 is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF_3, NH_2, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO_2NH_2, $CONH_2$, CO_2Me, phenoxy, O-pyridinyl, SO_2phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF_3-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

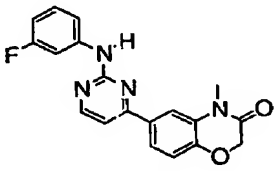
22. (Previously presented) The compound of claim 18 having the formula **IVa**, wherein R^X is hydrogen or optionally substituted C_{1-6}aliphatic; m is 0, 1 or 2; and ZR^5 is Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF_3, NH_2, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO_2NH_2, $CONH_2$, CO_2Me, phenoxy, O-pyridinyl, SO_2phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF_3-phenyl,

dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

23. (Previously presented) The compound of claim 1, selected from one of the following compounds:



IVa-1



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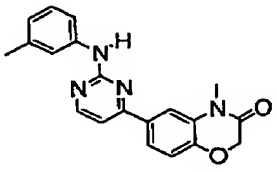

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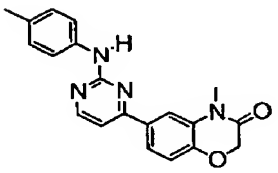

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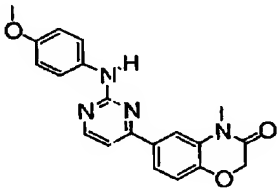

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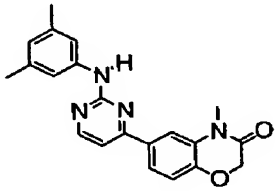

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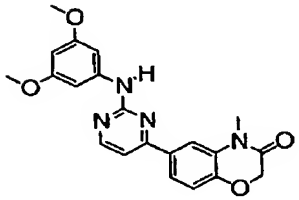

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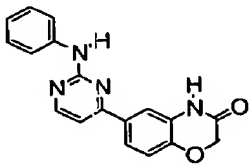

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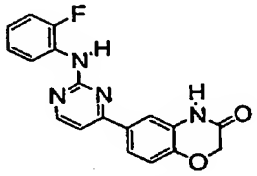

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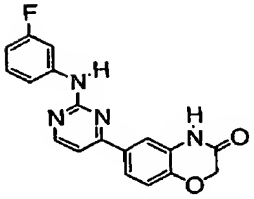

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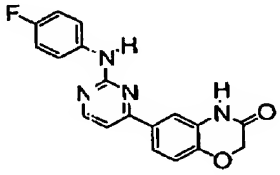

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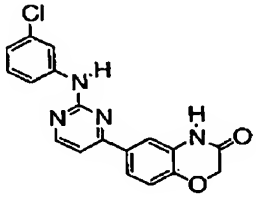

IVa-12

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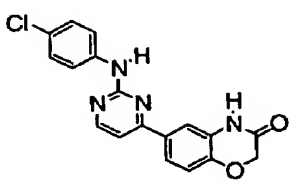

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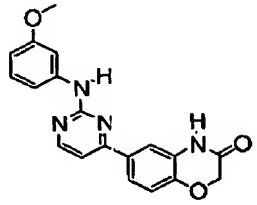

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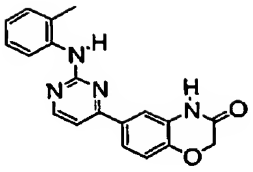

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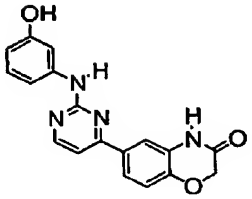

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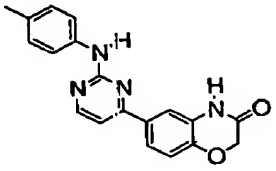

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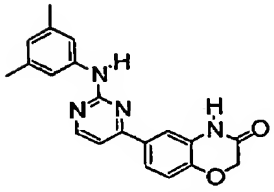

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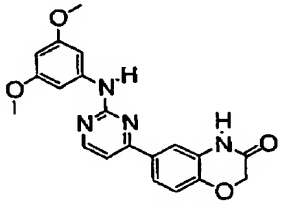

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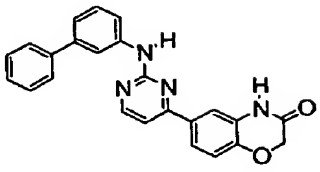

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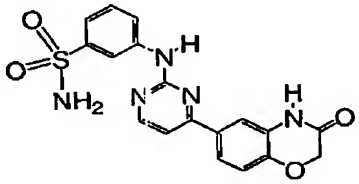
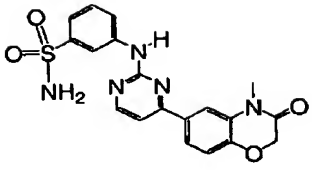
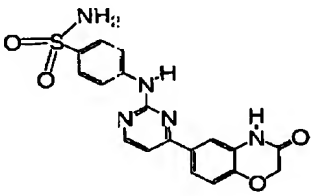


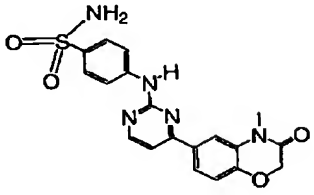
IVa-21



IVa-22



IVa-23



IVa-24

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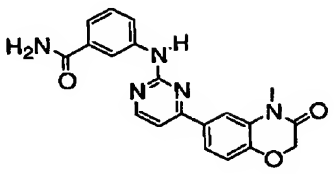
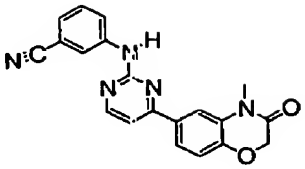
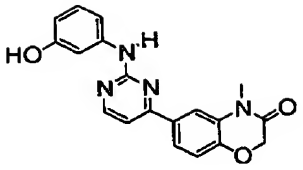


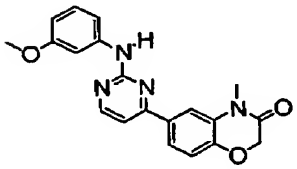
IVa-25



IVa-26



IVa-27



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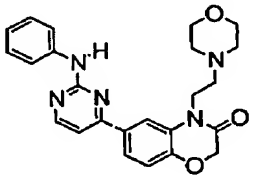

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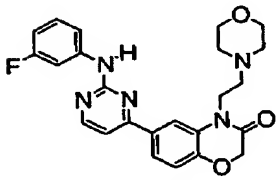

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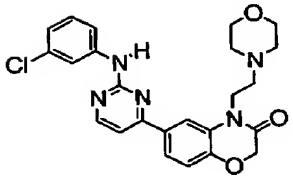
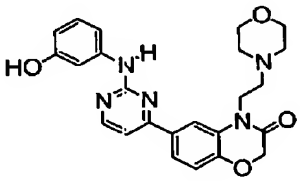
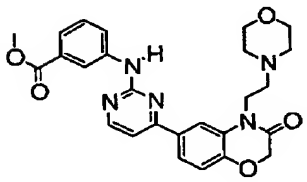


IVa-31



IVa-32



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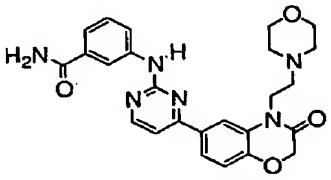

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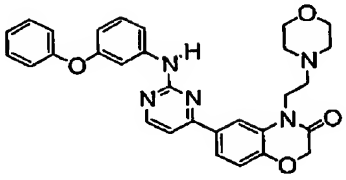

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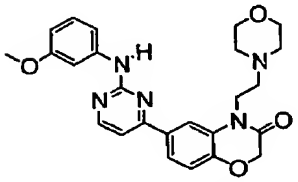

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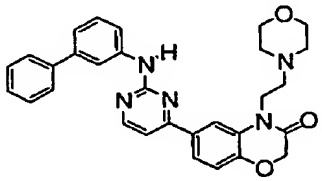

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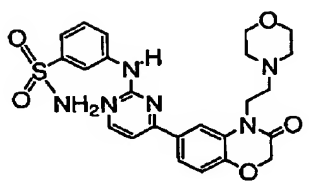
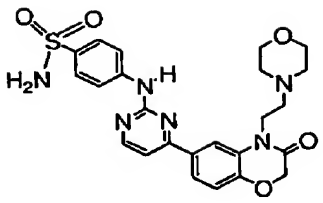


IVa-38



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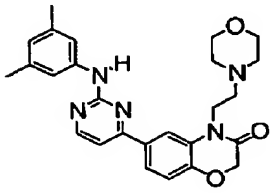

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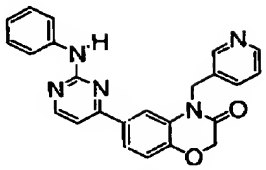

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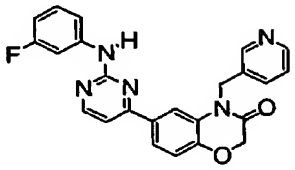

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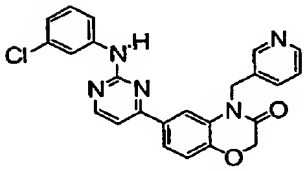

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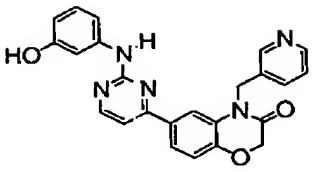

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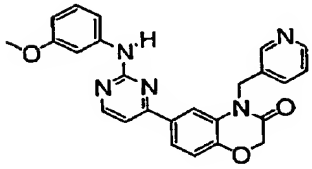

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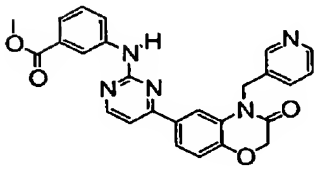

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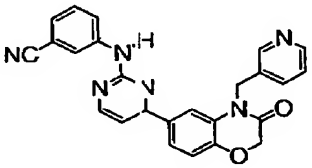

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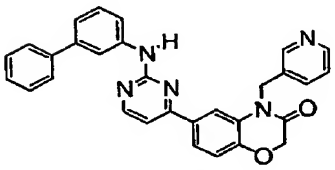
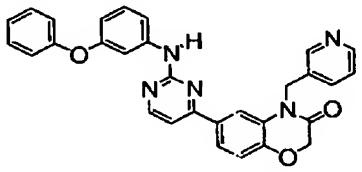


IVa-48



IVa-49

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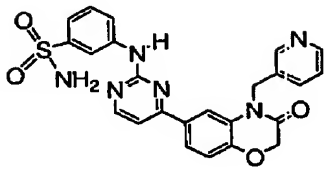
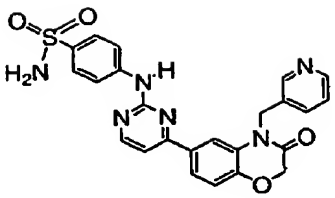
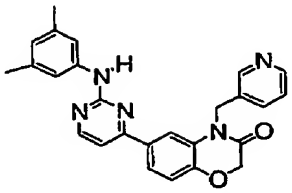


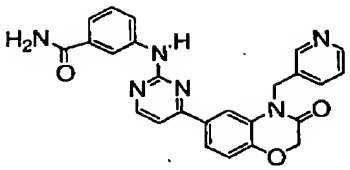
IVa-50



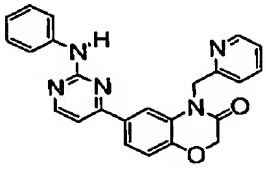
IVa-51



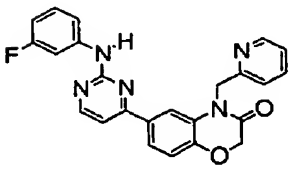
IVa-52



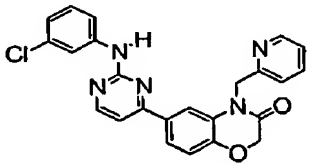
IVa-53



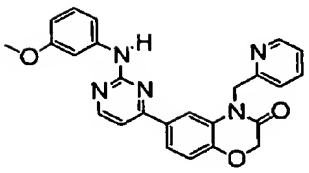
IVa-54



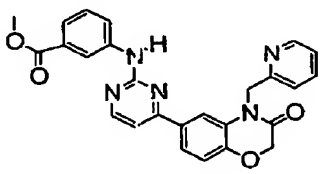
IVa-55



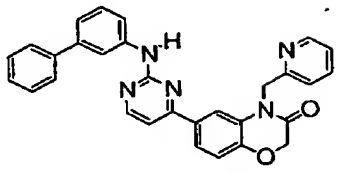
IVa-56



IVa-57



IVa-58



IVa-59

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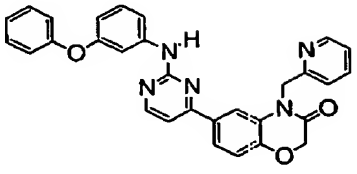
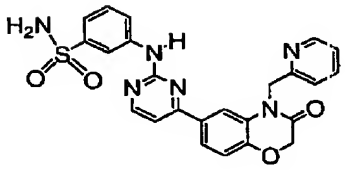
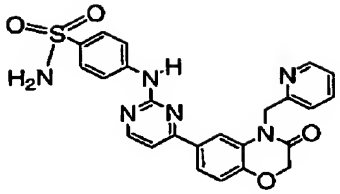


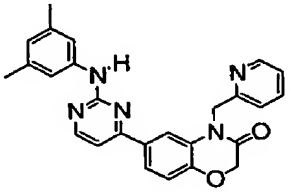
IVa-60



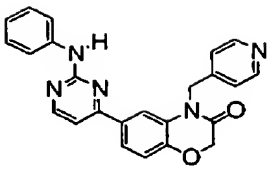
IVa-61



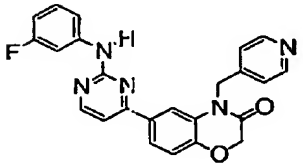
IVa-62



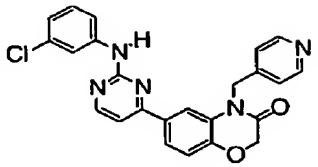
IVa-63



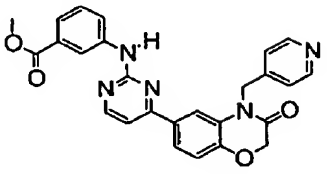
IVa-64



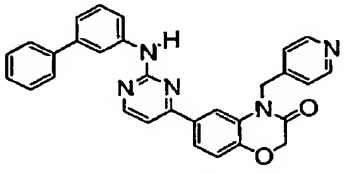
IVa-65



IVa-66



IVa-67



IVa-68

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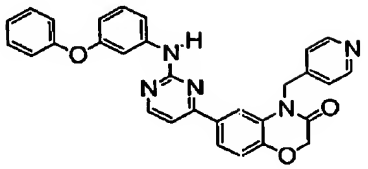
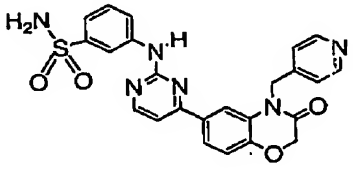
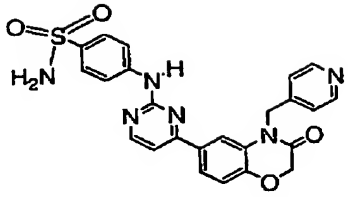


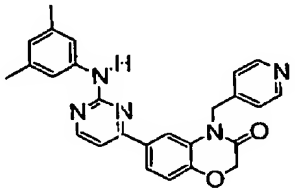
IVa-69



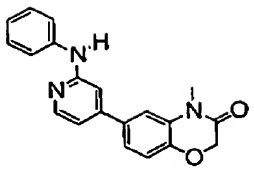
IVa-70



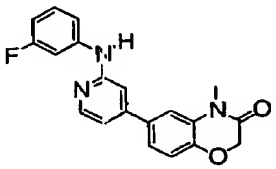
IVa-71



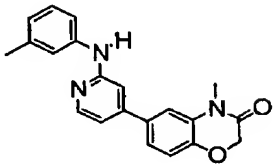
IVa-72



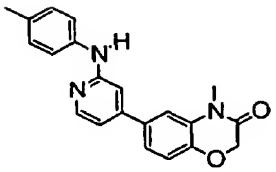
IVb-1



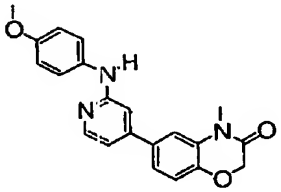
IVb-2



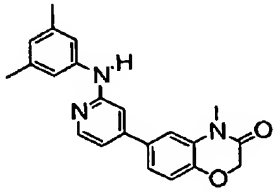
IVb-3



IVb-4



IVb-5



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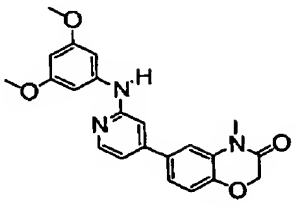
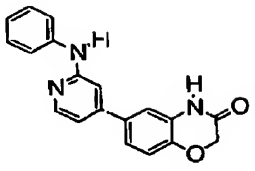
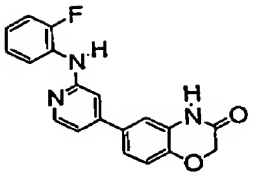


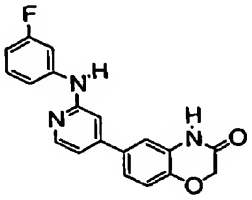
IVb-7



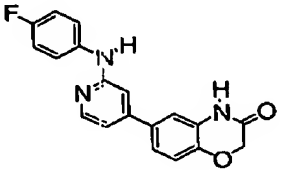
IVb-8



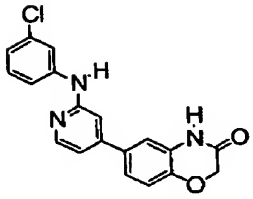
IVb-9



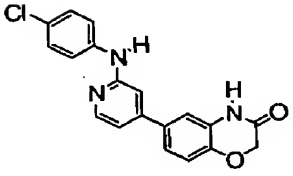
IVb-10



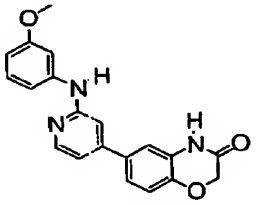
IVb-11



IVb-12



IVb-13



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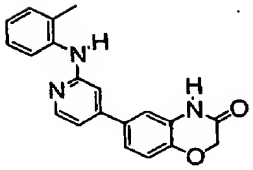

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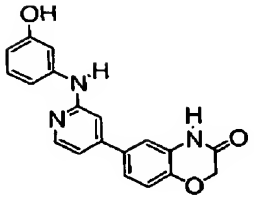
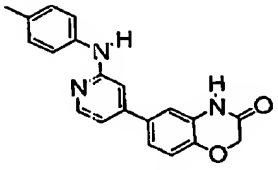
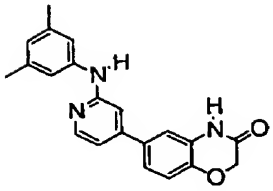


IVb-16



IVb-17



IVb-18

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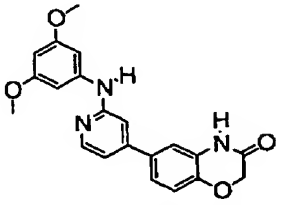
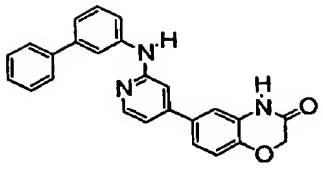


IVb-19



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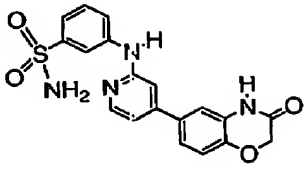
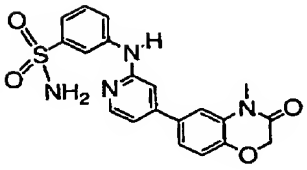


IVb-21



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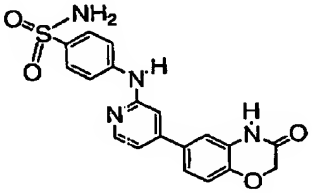

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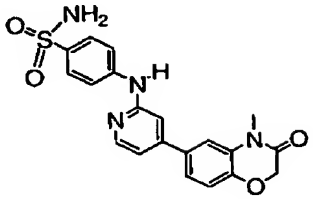
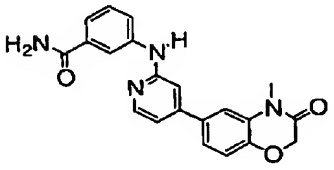


IVb-24



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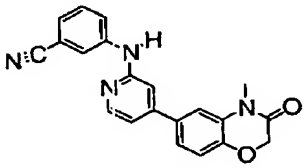
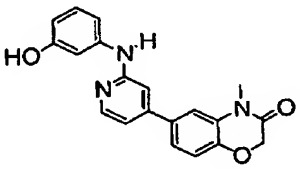
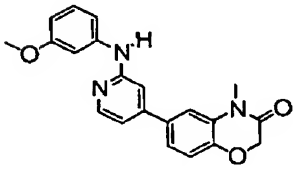


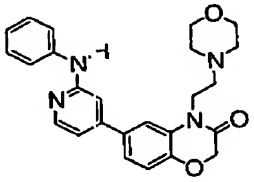
IVb-26



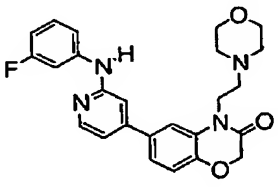
IVb-27



IVb-28



IVb-29



IVb-30

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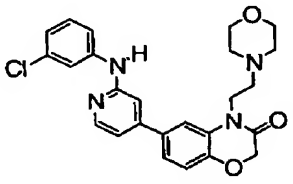
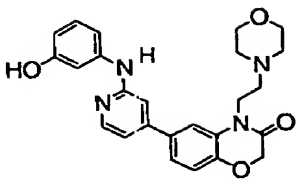
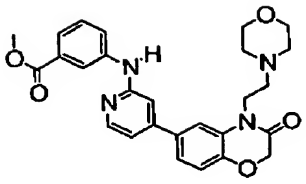


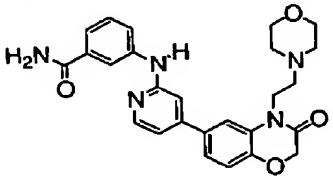
IVb-31



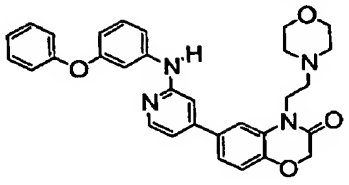
IVb-32



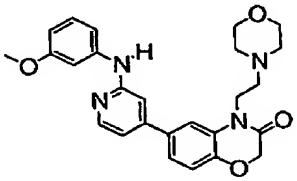
IVb-33



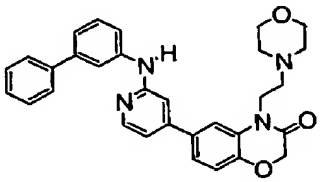
IVb-34



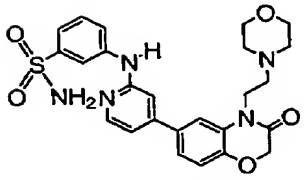
IVb-35



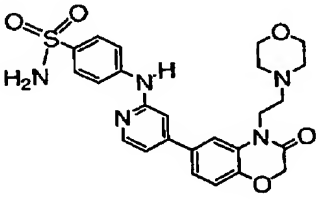
IVb-36



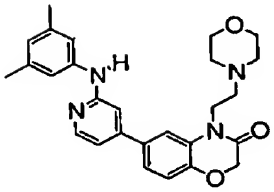
IVb-37



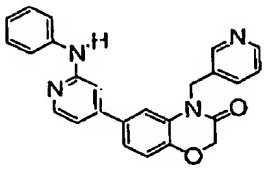
IVb-38



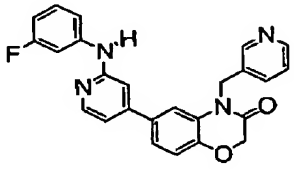
IVb-39



IVb-40



IVb-41



IVb-42

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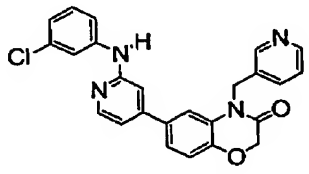
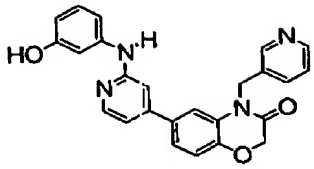
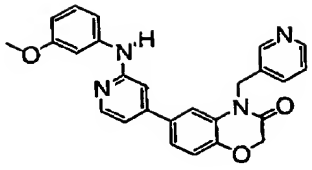


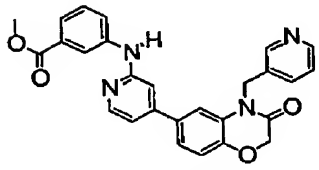
IVb-43



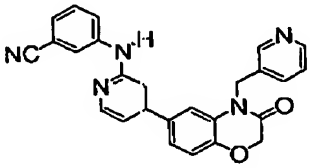
IVb-44



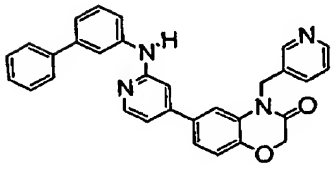
IVb-45



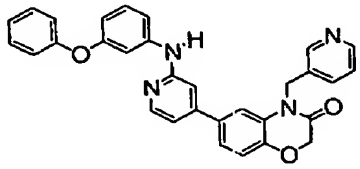
IVb-46



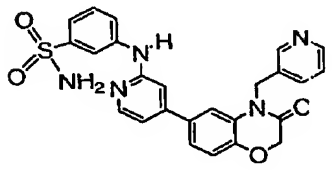
IVb-47



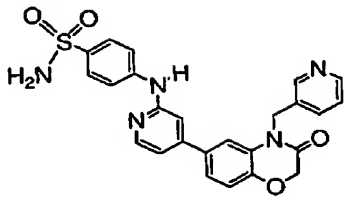
IVb-48



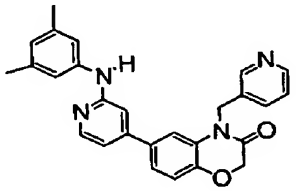
IVb-49



IVb-50



IVb-51



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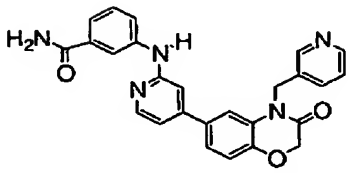
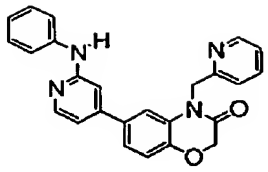
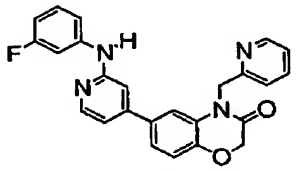


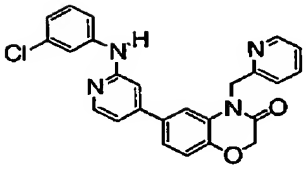
IVb-53



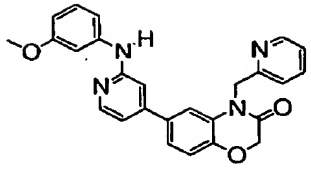
IVb-54



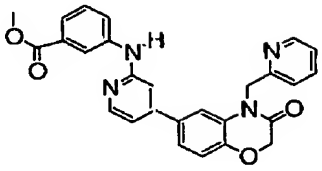
IVb-55



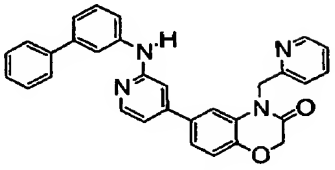
IVb-56



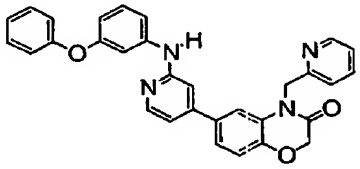
IVb-57



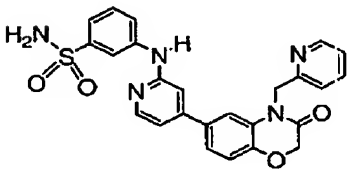
IVb-58



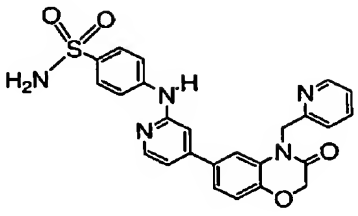
IVb-59



IVb-60



IVb-61



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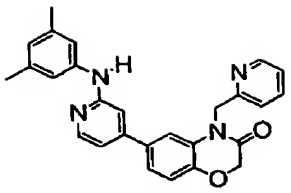
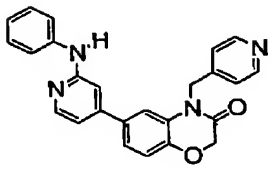
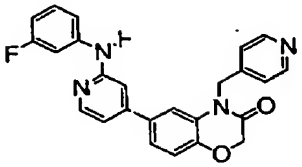


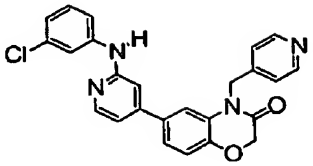
IVb-63



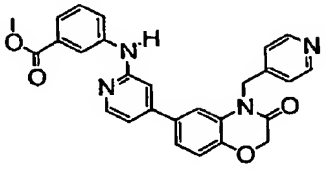
IVb-64



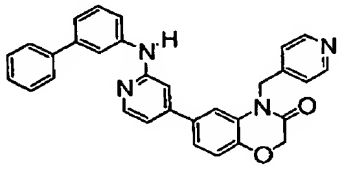
IVb-65



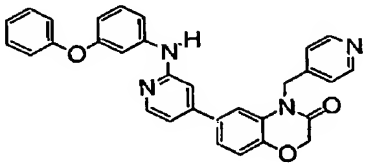
IVb-66



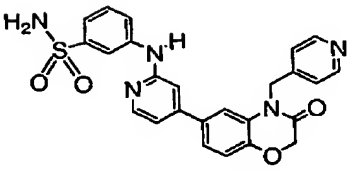
IVb-67



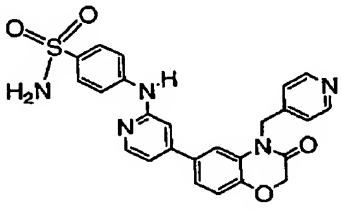
IVb-68



IVb-69



IVb-70



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Applicants: Randy S. Bethiel et al.
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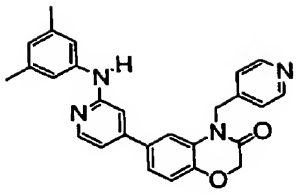

or **IVb-72.**

24. (Original) A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25-27. (Canceled)

28. (Currently amended) A method of treating or lessening the severity of a disease or disorder selected from an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, or rheumatoid arthritis, ~~or leukemia,~~ comprising administering to a subject in need thereof a compound of claim 1 or a composition comprising said compound.

29. (Currently amended) The method of claim 28, comprising the further step of administering to said patient an additional therapeutic agent selected from a ~~chemotherapeutic or anti-proliferative agent,~~ a treatment for asthma, an anti-inflammatory agent, or an immunomodulatory or immunosuppressive agent, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.